

PATENT SPECIFICATION

762,187



Date of Application and filing Complete Specification: Oct. 9, 1953.

No. 27854/53.

Application made in Germany on Oct. 9, 1952.

Complete Specification Published: Nov. 28, 1956.

Index at acceptance:—Class 2(3), C2B21.

COMPLETE SPECIFICATION

Metal Complexes of Hydrazide-Hydrazones and process for producing the same

5 We, FARBENFABRIKEN BAYER AKTIEN-
 GESellschaft, a body corporate organised
 under the laws of Germany, of Leverkusen-
 Bayerwerk, Germany, do hereby declare the
 invention, for which we pray that a patent
 may be granted to us, and the method by
 which it is to be performed, to be particularly
 described in and by the following statement:—

10 The present invention comprises metal
 complexes of hydrazones of hydrazides of
 heterocyclic carboxylic acids, the metal of
 which is selected from the 4th period and the
 2nd to the 8th groups of the Periodic system
 15 as defined below and a valence of which is
 bound to oxygen, together with procedure for
 producing such complexes.

It is known that the hydrazides of hetero-
 cyclic carboxylic acids and hydrazones pre-
 20 pared by the reaction of such hydrazides with
 aldehydes and ketones are of therapeutic sig-
 nificance and, in particular, that such deriva-
 tives of isonicotinic acid have been found to
 be effective for combatting tuberculosis in
 25 humans and animals. It is further known that
 hydrazides are capable of forming complexes
 with heavy metals and that in forming such
 complexes the hydrazides exert a reducing
 effect on the complex-forming metals at
 30 elevated temperature. Copper complexes of
 hydrazones of isocyclic carboxylic acid hy-
 drazides (Bui-Hoi, et al., Comptes Rendues
 des Seances de l'Academie des Sciences 235:
 330, 1952) have been prepared but the reac-
 35 tion was found by them to be specific for
 copper only and the resulting copper com-
 plexes have only slight therapeutic usefulness.

We have now found that new and highly
 useful complexes are obtained when hy-
 40 drazones of hydrazides of heterocyclic car-
 boxylic acids are reacted with compounds of
 complex-forming metals of the 4th Period and
 the 2nd to 8th groups of the periodic system,
 as shown on pages 154—5 of "Inorganic and
 45 Theoretical Chemistry" by F. Sherwood
 [Price 3s. 6d.]

Taylor (1947 edition). The discovery that the
 above metal complexes can be formed with
 ease and have new and valuable properties
 was surprising in view of the data presented
 in the literature, particularly because it was
 50 entirely unpredictable that the above metal
 complexes would exercise high therapeutic
 effects since the prevailing view is that the
 action of isonicotinic acid hydrazide and other
 tuberculostatic substances is due to the fact
 that metal is deemed to be withdrawn from
 the enzymatic system of the tuberculosis
 bacilli.

It is therefore, surprising that our new
 metal complexes have excellent tuberculostatic
 and veterinary utility. Our new compounds
 furthermore, in many cases, represent a
 marked change in solubility characteristics
 and thus, in accordance with the invention, it
 is frequently possible to prepare easily
 65 applicable water-soluble metal complexes—
 e.g., iron complexes—from hydrazide-
 hydrazones of heterocyclic carboxylic acids
 which are water-insoluble as such.

Heterocyclic carboxylic acids are used as
 70 starting materials in preparing our new
 hydrazide-hydrazones, for example, nicotinic
 acid, isonicotinic acid, alkylisonicotinic acids,
 pyromucic acid, the various quinoline car-
 boxylic acid isomers, thiophene carboxylic
 acid, pyrazole carboxylic acid and pyrimidine
 carboxylic acids. The heterocyclic carboxylic
 acids may, for example, be converted by way
 75 of their esters into the corresponding
 hydrazides and then reacted with any desired
 aliphatic, aromatic or heterocyclic aldehyde or
 ketone to produce the desired hydrazones.
 These hydrazide-hydrazones are reacted,
 according to this invention, with metallic
 compounds particularly metal salts, of com-
 85 plex forming metals of the 4th Period and
 the 2nd to 8th groups of the periodic system
 as defined. The hydrazide-hydrazone metal
 complexes so formed may be represented by
 the following type formula: 90